## REMARKS

This amendment is made to correct typographical errors, to resolve any confusion as to what the Applicants deem is their invention and to put the claims in condition for allowance. Support for the amendments can be found throughout the specification as filed. No new matter is introduced by this amendment.

**The Invention.**

The present invention provides a novel endoglucanase nucleic acid sequence, designated *egl8*, and the corresponding EGVIII amino acid sequence. The invention also provides expression vectors and host cells comprising a nucleic acid sequence encoding EGVIII, recombinant EGVIII proteins and methods for producing the same.

**Status of the Application.**

Claims 1-17, 19-20, 22-24, and 26 are pending in the application. Claims 1 and have been cancelled herein without prejudice. Claims 2, 4 and 26 have been amended herein to clarify what Applicants consider the subject matter of the invention. No new matter is introduced by these amendments.

Applicants have recognized the need for an updated Sequence Listing and will provide one shortly.

**Specification.**

The disclosure was objected to as containing an embedded hyperlink and/or other form of browser-executable code. Applicants have amended the specification to remove the hyperlinks. Withdrawal of the objection is respectfully requested.

**35 U.S.C. §112, first paragraph.**

*Claims 1-17, 19-20, 22 and 26*

Claims 1-17, 19-20, 22 and 26 stand rejected under 35 USC §112, first paragraph as failing to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. Specifically, the Examiner asserts that the claims are so broad because they encompass any variant or mutant polynucleotide encoding polypeptides that have 85%, 90% or 95% sequence identity to SEQ ID NO:5 (as noted above Applicants will provide a new sequence listing shortly) and that it would require undue experimentation to identify regions that could be changed. Applicants respectfully traverse.

First, Claim 1 has been cancelled without prejudice. Second, Claim 2 has been amended to recite 90%, 95% or 98% sequence identity to SEQ ID NO:5 or 95% sequence identity to SEQ ID NO:2. Applicants believe that a person skilled in the art would not require

undue experimentation to arrive at the claimed polynucleotides as claim 2 is now limited to Family 5 glycosyl hydrolases.

It is well settled law that the specification does not need to teach that which is well known in the art. Glycosyl hydrolases, including those in Family 5, are well characterized. As noted in the specification at page 24, the BLAST search performed by the Applicants indicated that the proteins with the highest identity are from glycosyl hydrolase Family 5. To be a member of this family one skilled in the art would recognize that the enzymes in this family display a common $(\beta/\alpha)_8$ fold structure and perform catalysis with net retention of anomeric configuration. Conserved residues are known for this family as well which will aid the skilled practioner in aligning sequences. Thus, this provides information on the various regions of the enzyme, and allows alignment and characterization of the identity of other proteins with the currently claimed EG VIII.

The Examiner asserts that the art is unpredictable. As a point of reference, Applicants direct the Examiner's attention to Mosimann et al., PROTEINS: Structure, Function and Genetics, vol. 23, pp. 301-317 (1995) (first page submitted herewith), wherein the author indicates that where sequence identity between the target and the template is greater than 70%, comparative molecular modeling is highly successful. (See abstract).

The Examiner further asserts that it is not routine to in the art to screen for multiple modifications. Applicants have provided guidance on applicable assays for measuring endoglucanase activity. Thus, one skilled in the art would be able to quickly determine if the protein possesses the required activity. As for the the number of changes, using any of the well known techniques in the art (e.g., MALDI-TOF) one can routinely sequence a protein, even large proteins, with ease. Once again, Applicants are not required to teach that which is well known in the art.

Withdrawal is respectfully requested.

*Claims 1-17, 19-20, 22 and 26*

Claims 1-17, 19-20, 22 and 26 stand rejected under 35 USC §112, first paragraph as allegedly containing subject which was not described in the specification in such a way as to convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse.

Applicants have cancelled claim 1 rendering the rejection moot for that claim. As the rejection relates to the other claims Applicant notes that the claims are direct to a specific set of naturally occurring enzymes with endoglucanase activity.

As noted above it is not necessary to teach that which is well known in the art. Persons skilled in the art are aware of the codons that encode the various amino acids. With the information on tertiary structure for Family 5 glycosyl hydrolases and the primary structure of EG VIII a person skilled in the art would be able to appreciate the Applicants could have had the claimed invention at the time the instant application was filed. Applicants note that it is not necessary under §112 that every claimed embodiment be specifically exemplified. Applicants respectfully submit that a skilled artisan would be able to glean from the specification the metes and bounds of the invention. Applicants also note that the number of polypeptides encoded by the polynucleotides encompassed by the present claims is finite and well within the skill of the ordinary artisan.

Withdrawal is respectfully requested.

**35 U.S.C. §112, second paragraph.**

Claim 2 and claims dependent therefrom stand rejected under 35 USC §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner asserts that Claim 2 is confusing due to the recitation of "Figure 2 (SEQ ID NO:2)".

Applicants have amended Claim 2 to clarify what Applicants believe is the invention. Withdrawal of the rejection is respectfully requested.

**35 U.S.C. §103.**

A *prima facie* case of obviousness requires the Examiner to cite to a combination of references which (a) suggests or motivates one of skill in the art to modify their teachings to yield the claimed invention, (b) discloses the elements of the claimed invention, **and** (c) provides a reasonable expectation of success should the claimed invention be carried out. Failure to establish any one of these requirements precludes a finding of a *prima facie* case of obviousness and, without more, entitles Applicants to withdrawal of the rejection of the claims in issue.[1] Applicants assert that the Examiner has failed to establish not one, but all three requirements as discussed below.

*Claims 1, 6 and 7*

The Examiner has rejected Claims 1,6 and 7 as being unpatentable over Bhikhabhai *et al.* (J. Appl. Biochem. (1984) 6:336-345) and Okada, *et al.* (Appl. Environ. Microbiol. (1998) 64(2):555-563). Specifically, the Examiner asserts that one skilled in the art would take the purified endoglucanase from Bhikhabhai *et al.* use the methods taught by Okada *et al.* and

obtain the poly nucleotide encoding EG VIII. The Examiner bases this objection on the assumption that one of the Bhikhabhai *et al.* endoglucanases (presumably EG II) and the presently claimed endoglucanase, referred to by Applicants as EG VIII, are one and the same. Applicants respectfully traverse the rejection.

Applicants have performed a BLAST search of the non-redundant protein database, conducted on September 12, 2001 with the EGVIII amino acid sequence indicated 52% identity with GenBank Accession Number AB021657 (endoglucanase II of *Trichoderma viride*), 51% sequence identity to GenBank Accession Number M19373 (endoglucanase EG-II precursor of *Trichoderma reesei*). See Specification at page 24, lines 15-24. That alone would indicate the two proteins are different.

The present EG VIII has an N-terminal sequence of Gly-Lys-Ile whereas the EG II of Bhikhabhai *et al.* has an N-terminal sequence of Glu-Pro-Gly. See Table I of Bhikhabhai *et al.* on page 343. Furthermore, the sequence Glu-Pro-Gly is not found in Applicants EG VIII. Thus, Applicants assert that the two proteins are not one and the same and that the skilled artisan would not combine the references.

As additional support Applicants have prepared the following Table to help the Examiner compare the amino acid composition of the various endoglucanases from the cited art and the presently claimed endoglucanase. Amino acids with more than 10 residues difference are highlighted. As can be seen, there are numerous residues in EG VIII that are not present at the same, or even similar, levels as in the Bhikhabhai *et al.* endoglucanases.

| Amino acid | N | Bhikhabhai N endo II | Bhikhabhai N endo III |
|---|---|---|---|
| Cys | 9 | 20 | 16 |
| Asp | 38 | 55 | 42 |
| Thr | 38 | 44 | 68 |
| Ser | 38 | 58 | 53 |
| Glu | 18 | 50 | 31 |
| Pro | 17 | 24 | 30 |
| Gly | 36 | 47 | 45 |
| Ala | 30 | 25 | 52 |

[1] *See e.g., Northern Telecom Inc. v. Datapoint Corp.*, 15 USPQ2d 1321, 1323 (Fed. Cir. 1990); and *In re Dow Chemical Co.*, 837 F.2d 469, 5 USPQ2d 1529 (Fed. Cir. 1988).

| Amino acid | N | Bhikhabhai N endo II | Bhikhabhai N endo III |
|---|---|---|---|
| Val | 22 | 19 | 32 |
| Met | 10 | 9 | 2 |
| Ile | 20 | 12 | 16 |
| Leu | 28 | 23 | 18 |
| Tyr | 15 | 23 | 9 |
| Phe | 18 | 9 | 8 |
| His | 5 | 6 | 3 |
| Lys | 20 | 9 | 9 |
| Trp | 6 | 7 | 7 |
| Arg | 7 | 7 | 9 |
| Gln | 12 | not reported in Bhikhabhai | |
| Asn | 23 | not reported in Bhikhabhai | |
| Total | 419 | 427 | 450 |

As the Bhikhabhai *et al.* reference fails to teach an endoglucanase with the same or even similar amino acid composition, one skilled in the art would not have been motivated to use the Bhikhabhai *et al.* endoglucanase(s) to obtain the inventive EG VIII in the present case and, thus, would not have combined Bhikhabhai *et al.* with Okada *et al.*

Therefore, Applicants assert that the rejection is in error. Applicants respectfully request that this rejection be withdrawn and the Claims be passed to allowance.

*Claim 26*

The Examiner has rejected Claim 26 as being unpatentable over Bhikhabhai *et al.* (J. Appl. Biochem. (1984) 6:336-345), Okada, *et al.* (Appl. Environ. Microbiol. (1998) 64(2):555-563) and Ward *et al.* (US Patent No. 6,265,204). Specifically, the Examiner asserts that one skilled in the art would have combined Bhikhabhai *et al.* with Okada, *et al.* to arrive at the polynucleotide sequence encoding the EG VIII endoglucanase and use the methods of Ward et al. to provide a vector and host cells to express the EG VIII endoglucanase. Applicants respectfully traverse the rejection.

For the reasons stated above regarding Bhikhabhai *et al.* and Okada, *et al.* these references fail to provide the required polynucleotide structure. Ward *et al.* does not correct the defect in Bhikhabhai *et al.* and Okada, *et al.*

The selection of the combination suggested by the Examiner is not fairly suggested in the prior art. The Examiner impermissibly picks and chooses ingredients without considering the invention as a whole, and looks suspiciously like hindsight reconstruction reached through the teachings of Applicants' disclosure. At best, the analysis is obvious to try. The "obvious to try" standard is one which has been thoroughly discredited. Indeed, an obviousness rejection is inappropriate, where the prior art [gives] either no indication of which parameters [are] critical or no direction as to which of many possible choices is likely to be successful." *In re O'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988); *Merck & Co., Inc. v. Biocraft Laboratories, Inc.*, 10 USPQ2d 1843, 1845 (Fed. Cir. 1989). Thus, Applicant respectfully requests that this rejection be withdrawn and the Claims be passed to allowance.

Accordingly, in view of the above remarks, it is submitted that this application is now ready for allowance. Early notice to this effect is solicited.

The Commissioner is hereby authorized to charge the fees necessitated by the filing of these documents, or to charge any additional fees under 37 C.F.R. 1.16 and 1.17, or to credit any overpayment, to Deposit Account No. 07-1048.

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Respectfully submitted,

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